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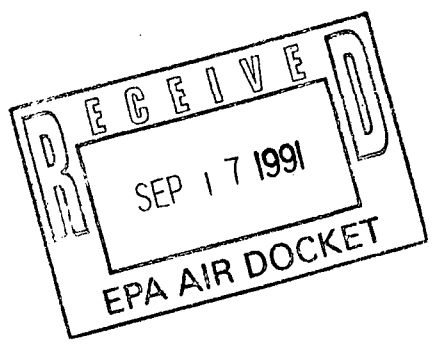
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Testimony of Albert C. Kolbye, Jr.

at EPA Hearing on MMT Waiver

September 12, 1991
Holiday Inn, Arlington, Virginia

Good Morning, Ladies and Gentlemen of the Panel and the Audience.

My name is Albert Christian Kolbye, Jr., and I speak with the training and experience of well over 30 years in biomedical and environmental health. I served 20 years in the United States Public Health Service Commissioned Corps, dealing mainly with problems of chemical safety, 13 of which with the U.S. Food and Drug Administration as a principal health advisor and manager on environmental chemicals in all relevant modes of human exposure. For 11 years I held the rank of Rear Admiral as an Assistant Surgeon General. I am a physician, also trained in public health and epidemiology, and have practiced environmental toxicology and risk evaluation for at least 25 years. I am also a lawyer. My role here is as an advisor to share with you what I know and what I see. I am retained by Chemetals, Inc. of Baltimore, Maryland for my professional time but not for advocating anything I do not believe. My Curriculum Vitae is attached to your copies of my prepared testimony.

I have at least 20 years experience in evaluating the potential risks to human health that might be associated with ingested, inhaled, injected, and topically applied chemical substances. These have included environmentally occurring compounds and those to which humans are exposed in occupational settings or in the practice of the medicinal sciences. My experience also includes being a responsible decision-maker in our efforts to prevent cadmium, lead and mercury poisoning which included extensive personal involvement in international approaches to these and many other problems.

I have been extensively involved in evaluating any potential public health risks of exposure to manganese compounds that might reasonably be expected to occur as a result of permitting the use of MMT as an additive to gasoline used in automobiles. I have reviewed all relevant documents of which I am aware.

I am here today to say that I see no public health problems that can reasonably be expected to occur if usage of MMT is approved. There really is no substantive scientific issue simply because the anticipated human exposures to manganese are so very small. There is no reason to expect or suspect problems with adults, children, pregnant women or their fetuses in relation to anticipated exposures related to usage of MMT.

Expected manganese residues in air from use of MMT in gasoline would approximate an increase of the background levels of 0.03 micrograms/cubic meter of air (m3) to about 0.05 micrograms/m3. It is fair to assume a total of 0.05 micrograms/m3 for the purpose of some calculations about potential risk. These exposure levels are at least 20,000 times less than those at milligram levels/m3 or higher which have been associated with manganese-induced diseases in occupational settings which involve extensive time-periods of

intensive exposures. There is an extremely wide margin of safety involved here.

A safety factor of 10 is very powerful if applied to a "no-adverse effect level" traditionally used in preventive toxicology for human data. Even more conservative is an additional 10-fold safety factor if only animal data are available, thus only 1% of a "no-observed adverse effect level" (NOAEL) in animals would be permitted for humans if an intentional food additive was involved. For many essential nutrients such as vitamin A, not even a 10-fold safety factor can apply because within that range, too little causes disease and too much causes disease. In the entire history of epidemiology and toxicology to protect people from exposures to chemical substances, no problems have arisen from using this approach to protecting public health, provided that reasonably accurate estimates of anticipated human exposure are available. (For known or suspected complete carcinogens or potent teratogens, additional safety factors have been used but are not relevant to manganese.)

Manganese is an essential and important micronutrient required for normal function of many enzymes in the mammalian body which includes us humans. Deficiency states are unlikely due to the ubiquitous dietary presence of substantial amounts of manganese but it should be remembered that less than desirable intakes may induce toxicity due to biological impairment from insufficient intake amounts. Below a certain intake, toxicity induced by deficiency of a required nutrient will occur. By implication, a wide margin of biological safety exists for manganese. Comparisons of lead toxicity to manganese biology are not appropriate to these proceedings, since lead is not an essential nutrient and insofar as we know today is toxic per se although the body has many effective biological defenses up to certain levels of exposure.

Only occupational inhalation exposures to humans in the range of milligrams/m³ sustained over many years have been associated with manganese toxicity.

The many animal toxicity studies referred to at the March, 1991 meeting in Research Triangle Park, NC, and elsewhere usually involved injections (by intravenous or subcutaneous routes of administration) of relatively massive amounts of manganese (milligrams/ kilogram of body weight) which are not relevant to low-level inhalation considerations. Such studies are not safety studies. They were designed to create toxicity in order to study biological endpoints of interest and mechanisms by which biological damage might be induced. Such studies must be considered in the context of the high dosage patterns employed by the researchers.

Epidemiological considerations concerning the information so far submitted to EPA do not suggest further need for large scale studies. Data exist which could receive further review to specify



certain details but there are no data to indicate trouble to be expected from usage of MMT. In fact, usage of MMT in Canada at higher levels than proposed for the USA have not been associated with any problems. Micro-environments can be monitored where needed to assure that inhalation exposures in such settings are not excessive.

Children are not expected to have any problems from these airborne exposures nor would pregnant women and their fetuses. These findings are evident from EPA's report of the conference in March 1991 at Research triangle Park in North Carolina.

For whatever reasons that underlie the safety factors that were applied by EPA to the estimated RfC, their total sum is not justified by factual science or public health experience. There is no substance known to humankind which requires more than a 1000-fold safety margin with reference to the lowest NOAEL as determined from relevant data in order to assure no significant risk to public health. This includes aflatoxin and 2,3,7,8 Tetrachlorinated Dibenzo Dioxin (TCDD). While safety margins approximating 5000 have been used for certain carcinogens, these considerations do not apply to manganese in any way. One can assume a "worst case scenario" for extreme interpretations of the available scientific evidence that there is a clearly apparent no observed adverse effect level (NOAEL) in humans of 0.5 milligrams/m³. There is at least a 100-fold safety margin from NOAEL human data, which is very reassuring indeed and by far exceeds the usual procedures involved to estimate and evaluate potential risks to public health.

CURRICULUM VITAE

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EDUCATION:

William Penn Charter School Philadelphia, Pennsylvania	H.S. 1953
Harvard College Cambridge, Massachusetts (Pre-Med, Pre-Law and Geology)	A.B. 1957
Temple University School of Medicine Philadelphia, Pennsylvania	M.D. 1961
University Hospitals Madison, Wisconsin (Internship - Mixed Medicine)	1962
School of Hygiene and Public Health The Johns Hopkins University Baltimore, Maryland	M.P.H. 1965
The School of Law University of Maryland Baltimore, Maryland	J.D. 1966
Federal Executive Institute Charlottesville, Virginia	1974

LICENSURES:

To Practice Medicine - State of Maryland
 since 1962
 To Practice Law - Maryland and District of
 Columbia since 1967
 Board Certification in Preventive Medicine
 and Public Health

PROFESSIONAL BACKGROUND:

Internship, University of Wisconsin,
 Madison - 1962
 Residency, Maryland State Department of
 Health - 1964
 United States Public Health Service,
 Commissioned Corps - 1962-1982:



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Heart Disease Control Program - 1962-1966
 Staff Director, Smoking & Health
 Program - 1967-1968
 Staff Director, Secretary's Commission
 on Pesticides - 1969
 Deputy Director, Bureau of Foods,
 FDA - 1970-1972
 Associate Bureau Director for
 Toxicological Sciences, Bureau of
 Foods, FDA - 1972-1982
 Assistant Surgeon General (07)
 USPHS - 1971-1982
 President - The Nutrition Foundation, Inc.
 1982-1984
 Past President - International Society of
 Regulatory Toxicology & Pharmacology
 1987-1988
 President - International Academy of
 Environmental Safety
 1989 to Present
 Director - Kolbye Associates
 1984 to Present

FELLOWSHIPS AND
MEMBERSHIPS:

Fellow of: American Academy of Clinical Toxicology
 American Public Health Association
 American College of Legal Medicine
 American College of Preventive Medicine
 International Academy of Environmental Safety

Co-Editor: Regulatory Toxicology and Pharmacology
 Academic Press

Member of: American Medical Association
 American Bar Association
 Maryland State Bar Association
 Maryland Medical Chirurgical Society
 Society of Toxicology
 Environmental Mutagen Society
 Society for Epidemiologic Research
 Society of Ecotoxicology and
 Environmental Safety
 New York Academy of Sciences
 Toxicology Forum
 Society for Preventive Oncology
 International Commission for Protection
 Against Environmental Mutagens and
 Carcinogens



CHAIRMANSHIPS OR
STAFF DIRECTORSHIPS:

The Surgeon General's Reports to Congress on the
Consequences of Smoking - 1967, 1968 and 1969
The Secretary's Commission on Pesticides and Their
Relationship to Environmental Health, DHEW - 1969
Secretary's Representative to the Interagency
Pesticide Agreement - 1970

The Health Hazards of Mercury, DHEW - 1971

Health Hazards Evaluation Board, Bureau of Foods,
Food and Drug Administration - 1972-1982

Research in Human Subjects, FDA - 1972-1982

Interagency Epidemiological Working Group on
Saccharin - 1976-1980

Interagency Working Group on Mechanically Deboned
Meat, U.S. Department of Agriculture - 1976-1977

WHO Scientific Consultant for Preparation of
Environmental Health Criteria for Nitrates,
Nitrites, and N-Nitroso Compounds, Environ-
mental Health Criteria 5, WHO Geneva - 1977

FD&C Red No. 40 Working Group - 1976-1981

Subcommittee 4 (Regulatory and Legislative)
International Commission for Protection Against
Environmental Mutagens and Carcinogens - 1978-1982

Interagency Working Group on Saccharin Epidemiology

Interagency Working Group on Nitrite Research

RECENT POSITIONS HELD:

Rear Admiral, USPHS - 1971-1982
(Assistant Surgeon General)

Deputy Director, Bureau of Foods, FDA - 1970-1972

Associate Bureau Director for Toxicological



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Sciences, Bureau of Foods, FDA - 1972-1982

President, The Nutrition Foundation, Inc.
Washington, DC - 1982-1984

PRESENTATIONS AND PUBLICATIONS:

Over 100 invited speeches and published papers concerning the safety of chemicals and foods, animals and human nutrition, and public policy issues and law.

(Detailed bibliography to be provided upon request.)